EXHIBIT B

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

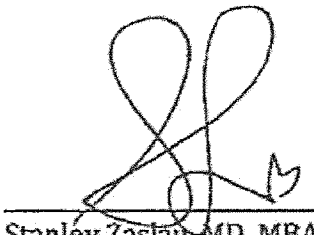
IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	Master File No. 2:12-MD-02327 MDL 2327 JOSEPH R. GOODWIN U.S. DISTRICT JUDGE
THIS DOCUMENT RELATES TO: *Mary Hendrix and Thomas Hendrix v Ethicon, Inc., et al* *Case No. 2:12-cv-00595*	

GENERAL AND CASE SPECIFIC REPORTS

OF STANLEY ZASLAU, M.D., MBA, FACS

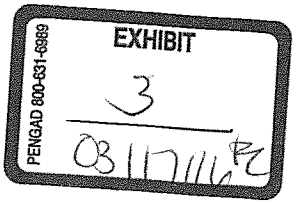
MARY HENDRIX

Prepared By:



Stanley Zaslau, MD, MBA, FACS

March 2, 2016



I make these reports in connection with the matter styled *Hendrix et al. v. Ethicon, Inc., et al.,* Case No. 2:12-cv-00595. I hold all the opinions stated herein to a reasonable degree of medical certainty; they are based on my education, training, experience, professional society guidelines, analyses, position statements and literature, the medical literature, TVT documents, depositions and other materials I have reviewed. A copy of my Curriculum Vitae is attached to this document as Exhibit A. A list of the materials I reviewed and relied on in reaching the opinions set out in these reports is attached as Exhibit B. My opinions, both general and case specific, are based on the information I have reviewed as of the date of this report. If I receive additional information before trial, I may form additional or modified opinions. In addition, should I perform an Independent Medical Examination on Ms. Hendrix, I reserve the right to supplement my report, as set forth in the parties' Stipulation and Agreement regarding the Independent Medical Examination of the plaintiff.

GENERAL REPORT

This report summarizes my qualifications, training and experience, and my opinions about the design of the TVT Retropubic device ("TVT") and more specifically whether the design of the TVT is reasonably safe for its intended use for the treatment stress urinary incontinence.

I. Background, Training and Experience

I received my undergraduate degree in biology and psychology from Boston University in 1988. I attended Hahnemann University School of Medicine and received my MD degree in 1994. I completed my internship in general surgery and urology residency training at Mount Sinai Medical Center (New York) in 2000. I completed an

additional year of training as part of the Consortium Group Urologic Surgical Associates in Brooklyn, New York, where I received advanced training in incontinence, voiding dysfunction, prosthetics and pelvic prolapse.

Upon completion of training in 2001, I accepted a position as Assistant Professor of Urology at West Virginia University. My practice area of focus was incontinence and voiding dysfunction. I achieved board certification in urology in 2003. I was promoted to Urology Residency Program Director and Associate Professor of Urology in 2005. I was promoted to Professor and Chief of the Division of Urology in 2010.

In 2013, I took and passed the inaugural subspecialty certification examination in Female Pelvic Medicine and Reconstructive Surgery and am currently the only such certified professional in the State of West Virginia. In 2013, I was named as the Associate Chairman of Education and Research for the Department of Surgery. My practice is still very active in incontinence, voiding dysfunction and sexual dysfunction in men and women. I serve as the Co-Director of the West Virginia University Center for Voiding and Sexual Dysfunction.

I am very active in treating patients with incontinence, voiding dysfunction and pelvic floor prolapse. I learned to perform the retropubic TVT procedure in residency (1996-2000) and was able to appreciate the ease of performing this procedure. I was also taught how to perform pubovaginal slings and came to appreciate the added morbidity associated with the abdominal approach to harvest fascia for these cases. Vaginal wall suspensions were also commonly performed during that time and their failure rates and complications of suture erosion and extrusion were also well appreciated by me.

During my year of advanced training, I assisted and performed many retropubic TVT procedures without any intraoperative complications and excellent post-operative results.

From 2001 to the present time, I have performed hundreds of TVT and TVT-O procedures. I am very familiar and comfortable with these procedures and have had excellent success with them. I have not had any bowel, bladder or vascular injuries. I carefully review with patients preoperatively, postoperatively and at each subsequent office visit all of the known risks and potential complications of pelvic floor surgery including incontinence, recurrence, voiding dysfunction, pain, sexual dysfunction, mesh erosion and extrusion. This has resulted in excellent long term patient satisfaction over 14 years.

I am being compensated for my work in this matter at a rate of $500 an hour. For work required to be turned around in 10 days or less, my rate increases to $750 an hour. I have given depositions and testified at trial as an expert witness within the past four years in the following cases: *Burkhart v. Life Chiropractic, Steward v. Bard, Weaver v. WVUH, and Edwards v. Ethicon.*

II. Summary of General Opinions

A summary of my opinions, as set forth in more detail later in this report, is as follows:

- Many women suffer from urinary incontinence, including stress and urge incontinence. Incontinence can be very detrimental to a woman's quality of life.

- There are non-surgical options for the treatment of stress urinary incontinence. However, non-surgical options are not always effective and many women ultimately seek surgical treatment after first considering or trying non-surgical treatments.
- Surgical options include Burch colposuspension and sling procedures, consisting of autologous fascia, cadaveric tissue, materials of other biologic origin, or macroporous, monofilament polypropylene. For many patients, surgery is the most effective treatment for stress urinary incontinence.
- Polypropylene mid-urethral slings like the TVT are widely recognized as the standard of care for treating SUI today. They have been extensively studied and authoritative professional organization statements and the medical literature endorse and recommend their worldwide use by physicians in clinical practice which reflect their utility to surgeons and usefulness to patients in the overall surgical armamentarium.
- The TVT system is one that I have used in my own clinical practice for many years. It is safe and effective as a treatment for SUI and is less invasive than other surgical treatments.
- All surgeries have risks, and surgeries for the treatment of SUI are no exception. The main risks associated with sling procedures are taught to surgeons in training, are discussed at professional conferences and are widely reported in the medical literature.

- Pelvic pain, dyspareunia and other pain is frequently found in women of various ages and in the general background populations. The causes are multiple, such as other medical conditions like interstitial cystitis, dysmenorrhea, prior surgery, musculoskeletal dysfunction, estrogen status and tissue pliability. The medical literature and my clinical experience demonstrate that many women presenting for urologic and gynecologic conditions, such as prolapse and incontinence, have these complaints at baseline.
- Urinary incontinence and pelvic floor prolapse can be associated with sexual dysfunction. Affected patients can complain of difficulty with sexual desire, arousal, orgasm, lubrication, pain and satisfaction.
- Risk factors for female sexual dysfunction include: post-menopausal status, degree of pelvic prolapse, concurrent medical problems such as hypertension, diabetes and thyroid disease, surgical menopause from hysterectomy and scarring from prior episiotomy and repair of tears during childbirth.
- Pelvic pain and other pain (inguinal and lower extremity related pain) are known risks of sling procedures (or any other vaginal surgery). However, pelvic pain, dyspareunia, and other sexual function factors such as fear of sex from incontinence, can also improve after sling procedures.
- Pain, sexual dysfunction, dyspareunia, and voiding problems are complications associated with any pelvic floor procedure, including MMK

procedures, vaginal or abdominal hysterectomies, bilateral salpingo-oopherectomies, anterior and posterior repairs.

- Another potential complication of synthetic sling procedures is the risk of mesh exposure or erosion. This uncommon complication can usually be treated very easily. The FDA has noted the mesh exposure rate for synthetic midurethral slings to be around 2%. (FDA 2013). This is consistent with larger reviews of the medical literature (Tommaselli 2015, Schimpf 2014, Novara 2008, Ford 2015, Unger 2014, Jonsson-Funk 2013, 2013, Nyguen 2012). Surgeon technique and volume also play a significant role in the incidence of complications. (Welk 2015). Welk and colleagues also discussed how most of the patients in their large population study who experienced a complication return to the implanting physician, which is contrary to a small tertiary study by Abbott (2014). In this latter paper, the authors noted that 50% of patients who sought treatment for a mesh complication at a tertiary care facility actually had their procedure performed at a different facility. The risk of erosion associated with sling procedures was well known among pelvic floor surgeons since the inception with the original TVT in 1998 and in fact before that as the medical literature reported on the use of synthetic materials to surgically treat SUI as well as potential complications including mesh exposure and erosion. In addition, all pelvic floor surgeons understand from their training and experience that no treatment is guaranteed to cure SUI and complications can always occur.

- It is important to discuss cytotoxicity with regard to mesh based slings. Wang (2004) reported a 2.4% rate of defective vaginal healing and a 1 % incidence of persistent delayed healing of the anterior vagina, 1 to 7 years after the operation. They believe that vaginal erosion may occur after delayed infection of the synthetic sling or prominent foreign body reaction, which leads to separation of the vaginal incision and sling erosion. In their study, six women had complete epithelialization over the mesh after 1 debridement of the vaginal tissue. They attribute these results to the presence of factors such as inadequate vaginal tissue coverage during the operation, rigidity of the mesh and its propensity for injury to adjacent tissues, or a site-specific, localized inflammatory response of the suburethral vagina is also plausible. This latter theory is important to note because in patients with complete epithelialization of the mesh who later had removal for other reasons, several patients displayed evidence of foreign body reaction, dense fibrosis, and occasional perivascular mononuclear cell infiltration. Thus, the inflammatory histologic reaction associated with slings can be present in slings that have extruded, have epithelialized or appear completely normal upon examination.
- Carcinogenesis has become another important point worthy of discussion. King (2014), Moalli (2014), and Linder (2016) reviewed the incidence of malignancy associated with pelvic mesh. No reports of malignancy have been reported in humans directly associated with these slings. The FDA, AUGS, and SUFU all have reported that midurethral slings are safe and

effective. We all believe that continued research is necessary but should be done in a scientific fashion to ensure its validity. As of this writing, there is no evidence to suggest that polypropylene midurethral slings have any association with malignancy.

- Laser Cut versus Mechanically Cut Mesh has become another important topic of discussion. I have only had three patients with mesh extrusions over a 15 year period and could not tell the difference between either mesh variation until I looked closely at the mesh with a magnifying glass. Personally, I have not seen any difference in complication rates between either variation of mesh in my clinical practice or in the peer-reviewed medical literature. In the many cases of urethrolysis I have performed over the years, I have not removed degraded particles of mesh or seen grossly altered structure of the knitting of the mesh in any of these specimens.
- Multiple studies and professional society consensus statements, surveys, and clinical practice guidelines, including but not limited to AUGS, SUFU, AUA, IUGA, NICE, EAU, and ACOG, have confirmed that midurethral synthetic slings are the treatment of choice and the standard of care for the surgical treatment of SUI. The 2014 AUGS and SUFU position statements highlight three important facts about synthetic mid urethral slings. (1) Polypropylene material is safe and effective as a surgical implant. (2) The monofilament polypropylene mesh MUS is the most extensively studied anti- incontinence procedure in history. (3) Polypropylene mesh midurethral slings are the standard of care for the surgical treatment of SUI

and represent a great advance in the treatment of this condition for our patients.

- As the first subspecialty boarded certified physician in Female Pelvic Medicine and Reconstructive Surgery, I have been able to provide care for, instruction in and surgical training in all aspects of this discipline.

III. General Opinions

A. Urinary Incontinence

Urine is produced by the kidneys and flows via peristalsis down the ureter to the bladder. Urine is then held in the bladder until voiding is undertaken. The urethra is at the most distal end of the urinary tract. Urine passes from the bladder through the urethra.

Urinary incontinence occurs when there is an involuntary loss of urine. This condition can be progressive, with significant worsening of symptoms over time. There are several types of urinary incontinence, namely urge incontinence, stress incontinence and mixed incontinence.

Urge incontinence is the involuntary loss of urine associated with increase in bladder pressure. The pressure increases to the point where voiding cannot be deferred and wetting accidents occur. The etiology of urge incontinence can be idiopathic or neurologic and also has significant associations with dietary intake.

Stress urinary incontinence ("SUI") is the sudden involuntary loss of urine in association with exertion, coughing, sneezing or other activity or movement.

If a patient has both urge incontinence and SUI she is described as having **mixed incontinence**.

Many factors have been associated with SUI. Risk factors include obesity, age, parity, vaginal delivery, menopausal status, diabetes, family history and history of hormone replacement therapy. Physical activity and smoking may also be risk factors. SUI may occur with injury or degeneration to the urethral support system or urethral sphincter mechanism; it is more likely that most women have elements of both problems. Women with a cystocele may have urethral hypermobility but not necessarily stress incontinence. If they have stress incontinence, they may have some urethral sphincter compromise along with the hypermobility. Trauma from obstetric delivery or another traumatic experience has been implicated in causing stress incontinence. Meyer and colleagues studied patients during pregnancy and 9 weeks postpartum. (Meyer, 1998, Obstetrics and Gynecology) They found that 36% of women who were delivered by forceps and 21% who delivered spontaneously suffered from urinary incontinence. Bladder neck mobility was significantly increased after all vaginal births, but bladder neck position at rest was only lowered in the forceps group. In addition, bladder neck mobility was significantly increased after all vaginal births, but bladder neck position at rest was only lowered in the forceps group. Women who underwent cesarean delivery were unaffected. Levator ani injuries can also occur after childbirth and result in later pelvic floor prolapse.

Stress urinary incontinence is common and is estimated to occur in approximately 1 of 3 women. Dooley and associates (2008) reported that nearly 50% of women over age 20 complained of incontinence symptoms. In this study, nearly 50% of patients reported pure SUI whereas 34% complained of mixed urinary incontinence. Nyygard and colleagues (2008) and Wu and associates (2010) reported that the prevalence of SUI

increases with age. According to an AUA foundation report in 2011, fewer than 50% of patients who suffer from incontinence report this to their healthcare provider and this may be due to embarrassment and shame. This is very unfortunate, because urinary incontinence can have a profound negative impact on women's well-being. Patients may experience isolation, limitation of social activities, professional limitations in terms of job advancement/promotion as well as impairment of intimate relationships. Patients may refrain from beneficial activities such as exercise because of fear of urine leakage.

The AUA guidelines were initially created in 1997 and revised in 2005, 2009 and 2012 to assist clinicians in the diagnosis and treatment of stress incontinence. The guidelines also suggest the importance of diagnosing concomitant pelvic prolapse as this can influence the modality of treatment selected for each patient. Evaluation and symptoms assessment must be undertaken for each patient including demonstration of incontinence with increasing abdominal pressure, frequency of urination, the severity of symptoms and degree of bother, the function of the urethral sphincter and the degree of hypermobility. Each patient should have a focused history to ascertain the type of incontinence present as well as the frequency, bother, severity of symptoms and impact of symptoms on lifestyle. Further discussion should focus on the patient expectations of treatment. Physical examination with objective demonstration of stress urinary incontinence is mandatory. Formal urodynamic evaluation may be of assistance in patients with complex presentations of incontinence such as the patient with mixed urinary incontinence. Patients must be counseled about comorbidities that can affect treatment outcomes. This allows the physician to plan an individualized treatment plan,

obtain an informed consent, project an estimate for a successful outcome and list potential complications.

B. Treatment Options for Stress Urinary Incontinence

Once diagnosed, the options for treatment of SUI include behavioral therapy or lifestyle changes, nonsurgical treatment and surgical treatment. Behavioral therapies include bladder training, fluid and diet management, smoking cessation, weight loss, avoiding bladder irritants and scheduled toilet trips. Nonsurgical options include Kegel exercises and the use of a pessary (a device inserted into the vagina to support the pelvic area and urethra). Kegel exercises are patient-taught exercises to identify the muscles of the pelvic floor that are involved in maintaining urinary continence. Patients are taught to squeeze and relax these muscles several times each hour, several times per day. When conducted over the long term, patients can see a modest improvement in urinary incontinence symptoms. However, success with Kegel exercises requires a motivated patient. Thus, there is a significant drop out rate for this therapy and many patients will go on to require additional therapies.

Pessaries are silicon, non-allergic devices that are placed into the vaginal canal to reduce pelvic floor prolapse. In general, these are used in patients with pelvic floor prolapse. Some patients with prolapse also complain of urinary incontinence. Pessaries can be considered for these patients. There is no difference between the types of pessary used when looking at patient satisfaction with this therapy. Pessaries need to be removed periodically to be cleaned and are then replaced. Many patients with pessaries drop out from this therapy because it is cumbersome and requires quite a bit of follow up care. The index patient to consider a pessary for is one with significant pelvic floor prolapse

who is a poor surgical risk because of multiple medical problems. It is most successful in the elderly patient.

Usually, nonsurgical or behavioral options are helpful only in milder cases of urinary incontinence, and only provide a lasting cure in a small subset of patients. For example, while many women experience some improvement from Kegel exercises, in my clinical experience few find this to be a permanent solution. Similarly pessaries are not convenient and can lead to vaginal discharge, pain, odor or bleeding. Many women discontinue pessaries or other similar nonsurgical treatments.

Biofeedback with pelvic floor muscle therapy teaches patients to identify muscles in the pelvic floor that are responsible for bladder and bowel continence. Through identification of these muscles, patients learn to control muscle function and possibly improve continence. This modality requires periodic therapy visits lasting approximately 30 minutes in duration for a several week cycle. Some improvement in urinary incontinence is noted for the motivated patient in the short term. Biofeedback can also be combined with electrostimulation of the pelvic floor muscles and short term studies show limited benefit through this additive therapy. However, with biofeedback (with or without electrostimulation), there is a significant dropout rate from treatment, and many patients will go on to other therapies.

Bulking agents like collagen are sometimes used to treat SUI. In this treatment, the agent is injected into tissues around the upper portion of the urethra via a cystoscope. This is not a permanent repair and is not as effective as surgery.

Surgery is the most effective and definitive way to treat SUI. Surgical options include colposuspension and sling procedures consisting of either rectus fascia or fascia

lata from the patient, cadaveric or biologic tissue, and macroporous, monofilament polypropylene used in the TVT.

The Burch colposuspension is an invasive surgical procedure involving an abdominal incision and identification of the pelvic bony ligamentous structures. Sutures are placed into the periurethral tissue and into the bony ligamentous structures. The long-term success rate for the Burch procedure is approximately 50-60%.

Albo and colleagues studied two groups of patients with SUI. (Albo, 2007) They noted a success rate of 49% for Burch and 66% for fascial slings in patients with SUI. They noted that more women who had a fascial sling had UTIs, difficulty voiding and post-op urge incontinence. The Burch procedure because of its abdominal incision, usually requires an inpatient hospital stay and has complications of wound infection, urethral injury and voiding dysfunction. As discussed below, the TVT has become much more popular than the Burch procedure and fascial sling because of its high efficacy, low morbidity, less invasiveness and ease of use.

Other types of surgical procedures used in the past to treat SUI, such as the Marshall-Marchetti-Krantz procedure, anterior colporrhaphy and needle suspension procedures, are not used very often today and are not recommended as the standard of care by medical associations because of a lack of efficacy and/or their complication profile.

C. Reasonableness of the TVT's Design for its Intended Use and its Utility / Usefulness

TVT was initially introduced in 1998 as a minimally invasive way to treat SUI. This was needed because of the surgical challenges with Burch and pubovaginal slings discussed above. Further, there were significant complications and lack of efficacy seen with needle suspension procedures (Raz Bladder Neck Suspension, Pledget-based needle suspensions and the four cornered vaginal sling). While short term (6-12 month) success was common with these procedures, longer term success was lacking. Further, there were significant complications noted with some of the procedures (Pledget-based needle suspensions) including erosion into the urethra and bladder. Thus, the need to invent a minimally invasive procedure was warranted. The TVT fulfilled this need by being minimally invasive and is easy to perform when indicated and when the guidelines specified by the manufacturers are followed accordingly. Patients certainly wanted a minimally invasive procedure that could treat their stress urinary incontinence and have them able to resume their usual daily activities with a short recovery period and periodic follow up with their physician to ensure that they were doing well. The design is safe and the short/long term efficacy are certainly present. To date, I have never had injury to any nerve, bowel or bladder (other than incidental isolated recognized trocar injury to the bladder, easily treated with short term catheter placement). I have had 3 cases of TVT mesh extrusion treated only with simple excision. My success rates are excellent and go out to 14 years with the use of TVT and TVT-O procedures with most patients dry or significantly still improved from baseline.

TVT implantation is technically easy to perform and easy to teach. The tape is fashioned under the urethra using small standard vaginal wall dissection that is only

1.5cm in length. This design is important because it involves minimal dissection to create a small tunnel for the sling to be placed into which follows the path of the urethropelvic ligament. As compared to the traditional pubovaginal sling, this dissection is quicker and easier to perform.

Explicit instructions via video and step by step instructions were provided by the manufacturer. Professional education courses were also provided by the manufacturer on how to safely perform this procedure. When I learned how to perform this in residency, I viewed the videos, which carefully explained all the necessary steps of the procedure.

Emphasis was placed on positioning the tape under the midurethra in a tension free manner using a clamp or Hegar dilator behind the tape so it does not obstruct the urethra. The use of the clamp/Hegar dilator is a critical portion of the procedure and allows the sling to sit without tension so that over time its incorporation into the tissue planes will be such that it mimics the location of the normal urethropelvic ligament and minimizes urethral hypermobility during stress. This is a critical design feature that physicians who perform the procedure must pay careful attention to in order to limit potential adverse effects such as voiding dysfunction, urethral pain and urethral erosion. The manufacturer's videos, IFU and subsequent articles by leading academic physicians have further reiterated this important concept. Instruction was also provided to slowly remove the plastic sheath to prevent shearing of the tape. This is well illustrated on the manufacturer's videos, and subsequent articles by leading academic physicians. It is well known that when the plastic tape is pulled quickly or is under tension that the mesh can shear. This concept is obvious to any physician who uses mesh in surgical procedures because when mesh is stretched, it loses its normal shape, pore size and can shear and

have portions flake off. Thus, the sheath over the mesh, when used according to the manufacturer's suggestion via video can easily be removed and this potential complication eliminated.

Synthetic slings are the most common type of surgical procedure performed today for SUI and monofilament, large pore polypropylene used in TVT is the most common type of synthetic material used in slings. Slings have a number of advantages over the Burch colposuspension procedure. In that procedure, the vaginal wall is attached to the Cooper's ligament adjacent to the public bone. A longer hospital stay is required. Surgical times and recovery times are longer. Wound complications and hernia can occur. The laparoscopic Burch is less invasive, but is more difficult to learn and perform, must be performed under general anesthesia and requires multiple abdominal incisions. Cadaveric slings, another surgical treatment option, are rarely used for a number of reasons, including lack of durability and rejection issues.

When compared to the pubovaginal sling, the TVT procedure produces superior cure rates at short term follow up and lower rates of adverse events. Sartori and colleagues (2008) studied 80 patients with SUI. Among those, 61 underwent TVT and 19 a pubovaginal sling. After 6 months, 96.7% of women with TVT and 89.5% of those with a sling thought they were healed from the procedure. Urinary retention was observed in 42% of the pubovaginal sling cases and 9.8% of the TVTs.

All SUI procedures have risks and potential complications; these procedures can and do fail in some patients. All surgeries involve some pain or discomfort and a surgery is never a guarantee of a cure or a pain-free postoperative period. Risks of SUI surgery include anesthesia risks depending upon type, bleeding and transfusion, hematoma,

infection, wound complications, urethral injury, organ and nerve damage, voiding dysfunction, urinary retention, urinary frequency and frequency, pain (including pelvic pain), dyspareunia (pain during sexual intercourse), inflammation, scarring, adhesions, urinary tract infections, fistula, DVT and other major surgical risks and need for additional or repeated surgical procedures. These are risks that all urologists, ob/gyns and urogynecologists are trained about in residency and fellowship. These risks do not need to be incorporated in the IFU because they must be considered and are known to any physician who undertakes to perform any pelvic floor surgical procedure.

Pelvic pain, dyspareunia and other pain is frequently found in women of various ages and in the general background populations. The causes are multiple, such as other medical conditions like interstitial cystitis, dysmenorrhea, prior surgery, musculoskeletal dysfunction, estrogen status and tissue pliability. The medical literature and my clinical experience demonstrate that many women presenting for urologic and gynecologic conditions, such as prolapse and incontinence, have these complaints at baseline. Urinary incontinence and pelvic floor prolapse can be associated with sexual dysfunction. Affected patients can complain of difficulty with sexual desire, arousal, orgasm, lubrication, pain and satisfaction. Risk factors for female sexual dysfunction include: post-menopausal status, degree of pelvic prolapse, concurrent medical problems such as hypertension, diabetes and thyroid disease, surgical menopause from hysterectomy and scarring from prior episiotomy and repair of tears during childbirth. Pelvic pain and other pain (inguinal and lower extremity related pain) is a known risk of sling procedures (or any other vaginal surgery). However, pelvic pain, dyspareunia, and other sexual function factors such as fear of sex from incontinence, can also improve after sling procedures. Of

course, there are patients who have pelvic pain in addition to urinary incontinence and desire their incontinence treated. In the appropriate patient with urethral hypermobility and documented stress urinary incontinence, a TVT can be considered a first line treatment. Such patients may achieve a cure of their stress incontinence while their pelvic pain worsens. In my experience, this worsening of pelvic pain following TVT is unrelated to the TVT but rather is due to pelvic floor neural hypersensitivity. These patients with chronic pain and stress incontinence who desire a TVT (or another surgical treatment for incontinence) are warned about the possibility of worsening of pelvic pain after the anti-incontinence procedure.

Another potential complication of synthetic sling procedures is the risk of mesh exposure or erosion. That uncommon complication can usually be treated very easily. The risk of erosion associated with sling procedures was well known among pelvic floor surgeons since their inception with the original TVT in 1998 and in fact before that as the medical literature reported on the use of synthetic materials to surgically treat SUI as well as potential complications including mesh exposure and erosion. In addition, all pelvic floor surgeons understand from their training and experience that no treatment is guaranteed to cure SUI and complications can always occur.

Multiple studies and professional society consensus statements have confirmed that midurethral synthetic slings are the treatment of choice and the standard of care for the surgical treatment of SUI. The 2014 AUGS and SUFU position statements highlight three important facts about synthetic mid urethral slings. (1) Polypropylene material is safe and effective as a surgical implant. (2) The monofilament polypropylene mesh MUS is the most extensively studied anti- incontinence procedure in history. (3)

Polypropylene mesh midurethral slings are the standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients.

CASE SPECIFIC REPORT

I. Overview of Ms. Hendrix's Medical Condition

A. Past Medical History

Ms. Hendrix has an extensive medical history which includes reports of the following:

1. A diagnosis of breast cancer of the left breast in 2006. She underwent a lumpectomy followed by radiation. She developed significant complications of this radiation therapy including GERD, vocal cord dysfunction, and a nutcracker esophagus. She was diagnosed with cancer in her right breast in 2009. This in turn led to a bilateral mastectomy. (HENDRIXM_VUMC_102-103).

2. Hysterectomy and an MMK procedure in the 1980s (HENDRIXM_BHL_6-9).

3. Prolapse of vaginal vault after hysterectomy (July 2008) (HENDRIXM_LOUPW_3-4).

4. History of urinary tract infections both before her mesh was implanted and after it was explanted. (HENDRIXM_HHA_1, 18, 21-23, 28, 30, 33,40, 42; 118-19, 125; Dr. Adams depo. at 22-24; 26-28; 30; 32-36; 43-45; Plf's depo. at 45-46).

5. Peripheral Neuropathy and Reactive Hypoglycemia (HENDRIXM_VUMC_92).

6. Osteoarthritis (HENDRIXM_VUMC_102).

7. Raynaud's syndrome (HENDRIXM_VUMC_102).

8. Ill-defined autoimmune connective tissue disease disorder (HENDRIXM_VUMC_566-67).

9. Rheumatoid arthritis (Plf's depo. at 24-25).

10. Sleep apnea (HENDRIXM_VUMC_751-72).

11. Ataxia and other gait issues (HENDRIXM_VUMC_124-28).

12. Memory problems (HENDRIXM_VUMC_124-28).

13. Episodes of blacking out (HENDRIXM_VUMC_101-105).

14. Conversion disorder (HENDRIXM_VUMC_104-105).

15. Ménière's disease (HENDRIXM_VUMC_1660-63).

16. Stress urinary incontinence (HENDRIXM_BHL_4) (HENDRIXM_HUBBC_2-11).

17. Cholecystectomy (HENDRIXM_BHL _83-84).

18. Chronic obstructive pulmonary disease (HENDRIXM_VUMC_102).

B. Review of Medical Records Related to Implantation and Explantation of TVT Device

Ms. Hendrix started having urinary incontinence with cough, sneeze, and lifting in the 1980s, after the birth of her last child. The leakage was such that she was forced to wear two panty liners per day (Plf's depo. 86). Dr. Louis Kirtley diagnosed her with classic and chronic stress urinary incontinence, and on May 17, 1986, he performed a bilateral modified Marshall-Marchetti procedure at the same time as an abdominal hysterectomy, secondary to chronic menometrorrhagia and chronic dysmenorrhea. The pelvic exam performed before these procedures were suspicious for uterine fibroids, and the vaginal exam showed anatomical findings of prominent urethral excursion and a small cystourethrocele. (HENDRIXM_BHL 5-7.) Ms. Hendrix was 32 at the time of these procedures. Permanent sutures are often used in MMK procedures, which can have issues with erosion and extrusion. Patients after MMK procedures can have long lasting voiding dysfunction including urinary urgency, frequency and recurrent UTIs. Ms. Hendrix had #7, 0 Vicryl sutures placed during the MMK procedure.

Ms. Hendrix's stress urinary incontinence returned, and she sought treatment from John G. Hubbard, MD, on July 17, 2006, after experiencing stress urinary incontinence

for the preceding seven to eight years, with the condition worsening in the preceding two years. Once again, she was forced to wear panty liners, as she was leaking with bending, lifting, laughing, coughing, and sneezing (Plf's depo. at 117-120). She told Dr. Hubbard that she believed her problem with urine leakage was related to the onset of menopause.

Dr. Hubbard's initial exam revealed a grade 1 cystocele, mild rectocele, and poor pelvic tone. Ms. Hendrix weighed 176 pounds and she was 5'5" tall. Dr. Hubbard prescribed Neurontin and ordered a renal ultrasound and a CT exam of the abdomen and pelvis, which showed no evidence of a renal mass. A urodynamics study revealed incomplete bladder emptying and Type II stress urinary incontinence provoked by cough and Valsalva. Details of the urodynamics revealed a physiologic bladder capacity of 200 cc and a maximum flow rate of 5 cc/sec. This is a very slow flow rate which suggests urethral obstruction. This can be expected because she had an MMK procedure. The bladder was trabeculated to +1/+3 suggesting longstanding bladder dysfunction. Given her documented SUI, she was an excellent candidate for a TVT sling.

Dr. Hubbard through his office notes indicated that he explained the TVT procedure to her in detail, including that the mesh implant was meant to address her stress urinary incontinence and could actually make her urinary frequency and urgency. He also discussed with her the "extreme importance" of commencing pelvic floor therapy three months after the procedure. His notes reflect that she understood the complications of frequency, urgency, retention, and a small chance of bladder and bowel perforation. (HENDRIXM_HUBBC 2-12).

Ms. Hendrix returned to Dr. Hubbard's office on September 7, 2006, to learn how to perform self-catheterizations. (HENDRIXM_HUBBC 13.) This is noteworthy as he

was already anticipating the potential for post-operative voiding dysfunction in patients who undergo pelvic floor surgery. He is to be commended for this as not many physicians teach self intermittent catheterization to patients before their scheduled pelvic floor surgeries. Dr. Hubbard also told Ms. Hendrix that she has pelvic muscle wasting. This may have been caused by her pregnancies, lack of exercise and getting heavy. (Dr. Hubbard depo. at 52.)

Dr. Hubbard implanted a TVT device into Ms. Hendrix's pelvis on September 14, 2006. Dr. Hubbard's operative report states that Ms. Hendrix has been totally evaluated including urodynamics and cystoscopy, and found to have significant leakage. His note reflects that Ms. Hendrix understood that the procedure and elected to proceed with procedure. No complications of the surgical procedure were noted, and she did not have to catheterize after surgery. From the review of the operative note, it appears that Dr. Hubbard followed all of the key steps of the TVT IFU. (HENDRIXM_HUBBC 18-19; Dr. Hubbard depo. at 56.). Ms. Hendrix returned for a post-operative visit 14 days later (on September 28, 2006). She reported having dysuria and stated she thought she had a UTI. Ms. Hendrix denied having urinary incontinence. Her surgical incisions and sutures "looked good." A urinalysis was "positive." Dr. Hubbard recommended again that pelvic floor rehabilitation measures should begin three months after implantation of the TVT device. (HENDRIXM_HUBBC_20.)

Ms. Hendrix returned for a follow-up visit on October 9, 2006. She complained of "burning," presumably with urination since the TVT was implanted. She stated that she had taken Proquin for three days about 10-to-11 days prior to her October 9, 2006 appointment. Dr. Hubbard also noted 100ccs of urine residual, which was the same as

before the surgery. Dr. Hubbard prescribed Macrobid for 10 days. (HENDRIXM_HUBBC_21-23; Dr. Hubbard depo. at 57-59).

Ms. Hendrix returned to Dr. Hubbard's clinic on November 13, 2006. She complained of a possible UTI, off and on since the last visit, and burning with urination. There was no indication that her stress urinary incontinence had returned. The diagnosis was chronic cystitis and Dr. Hubbard recommended a repeat cystoscopy. (HENDRIXM_HUBBC_ 26).

Ms. Hendrix returned to the clinic two weeks later (on November 27, 2006). She described having persistent complaints of burning with urination despite the administration of the antibiotic and the use of Pyridium. A urine culture taken on this date later showed no growth. Dr. Hubbard's diagnosis following this visit was chronic cystitis and incomplete bladder emptying. He recommended that Ms. Hendrix continue taking Pyridium on an as-needed basis, and he also instructed Ms. Hendrix to continue taking Macrobid twice daily. (HENDRIXM_ HUBBC_28-30).

Ms. Hendrix returned to the Hubbard Clinic approximately 5 months later (on June 4, 2007). (HENDRIXM_HUBBC_31-34). She had undergone radiation treatments for breast cancer since her prior visit to Dr. Hubbard in November. It is known that radiation treatments either directly (from the radiation) or indirectly (from psychosocial stress) can worsen bladder function with an increase in urinary urgency and frequency. She was referred by Dr. Adams, her family practitioner, and she reported that a few days earlier, she had sudden onset of urinary frequency and burning, bladder discomfort and flank pain. She did not report any stress urinary incontinence. A routine urinalysis in Dr. Hubbard's office on June 4, 2007 was positive for leukocytes, protein and nitrites. A

urine culture collected at the time of this visit later revealed greater than 100,000 CFU per milliliter of Proteus mirabilis. (HENDRIXM_HUBBC_33).

Dr. Hubbard performed another cystoscopy on June 6, 2007. No leakage was demonstrated with coughing or straining, no erosions were visualized, and there was no obstruction. Important findings included that her first bladder sensation was at 50 cc. She had an unstable bladder capacity during bladder filling at 100 cc and had a bladder capacity of less than 200 cc. These findings are very significant because it underscores the underlying problem with Ms. Hendrix. She has a sensory neuropathic small bladder capacity. This was noted preoperatively before her sling was placed and is similar with these findings. These findings can relate to an underlying Painful Bladder Syndrome/Interstitial Cystitis (PBS/IC) or from sutures from her MMK procedure injuring nerves to the urethra/pelvic floor. At this visit, Dr. Hubbard performed a pelvic exam that showed mild anterior wall prolapse.

Ms. Hendrix returned to the office for a routine follow-up visit on June 12, 2007. She noted that her infection was gone. There was no report of any SUI. Ms. Hendrix was given counseling regarding possible prevention of recurrent infections, including the importance of emptying her bladder at least 20 minutes after sexual activity, advice to void twice with each micturition and the use of probiotics. (HENDRIXM_HUBBC_38-40; Dr. Hubbard depo. at 64-65).

Ms. Hendrix returned to the clinic on July 2, 2007, complaining her symptoms of urinary frequency and bladder discomfort had returned. She stated that antibiotics were not helping these symptoms. Dr. Hubbard recommended a cystoscopy with dilation under anesthesia. (HENDRIXM_HUBBC_41-44). This was performed on August 1,

2007. Ms. Hendrix's urethra could be easily dilated with a 30 French catheter. There was no evidence of a urethral contracture due to the adjacent TVT sling. No mention of mesh extrusion or erosion was noted. Debris in the floor of the bladder was noted. This was interpreted as indicating that Ms. Hendrix was not completely emptying her bladder. On cystoscopy, there was no evidence of mesh erosion into the bladder. (HENDRIXM_HUBBC_50, 45).

Approximately 2 weeks after the preceding procedure, Ms. Hendrix saw an infectious diseases specialist (Dr. Xia). He concluded that an anatomical problem was the cause of Ms. Hendrix's recurrent UTIs after performing a physical exam and reviewing Ms. Hendrix's history and laboratory data. This anatomical problem can be related to the seven 0" Vicryl urethral sutures placed for her MMK which resulted in her initial cystoscopic findings of bladder trabeculation +1/+3 and low urinary flow rate. (HENDRIXM_CID_4-5).

At a later visit, Ms. Hendrix presented to the Hubbard Clinic on October 8, 2007 for her annual exam. She denied having problems with urinary retention, dysuria, hematuria, frequency, or a vaginal discharge. However, she reported having dyspareunia. This is one of only two such instances in the medical records where she noted dyspareunia. She was advised to use a lubricant (KY jelly) and topical vaginal estrogens for these symptoms. (HENDRIXM_HUBBC_51-55).

In the time period from 2008 to 2009, Ms. Hendrix has a decline in her overall medical health with worsening nutcracker esophagus, vocal cord dysfunction, COPD, shortness of breath, and chronic joint pain. On May 13, 2009, Ms. Hendrix was seen in a rheumatology clinic at Vanderbilt University. Records from this visit noted that Ms.

Hendrix's chief complaints were shortness of breath and chronic joint pain in her knees and hands. These records further note that Ms. Hendrix had stated that she had felt "healthy and well" until November 2006 when she underwent a lumpectomy for breast cancer that was subsequently treated with radiation treatments. Ms. Hendrix also reported having other problems, including sleep apnea, chronic dry eyes, gastro-esophageal reflux disease, and a positive anti-nuclear antibody blood test. The specialist who saw her indicated that the preceding complaints and findings could signify the presence of an autoimmune condition, but that diagnosis could not be confirmed at that point in time. Ms. Hendrix weighed 201 pounds at this visit. As mentioned previously, these conditions, and the presence of a possible autoimmune condition can be associated with PBS/IC. Ms. Hendrix has many of the features of this condition which include chronic urinary urgency, frequency, pelvic pain and the characteristic urodynamic findings of a small bladder capacity.

On Aug. 25, 2009, Ms. Hendrix was diagnosed with cancer in her right breast. A bilateral mastectomy was performed on Sept. 15, 2009. (HENDRIX_VUMC_1110, 838901). This procedure and its recovery can certainly be stressful. In patients with known PBS/IC, it is not uncommon to see their bladder symptoms worsen during the recovery period from invasive surgical procedures. This can persist for many months despite treatment for the underlying symptoms. Worsening urinary frequency, urgency and dysuria can be expected in such patients.

In February 2011, Ms. Hendrix was admitted into the hospital by Dr. French for complaints of left flank pain, dysuria, and hematuria. A urine culture revealed Klebsiella species sensitive to Rocephin. Ms. Hendrix received IV antibiotics, and a urologic

consult was ordered. Complicated UTI infections would not be unexpected in patients with significant medical problems such as seen with Ms. Hendrix. These can happen regardless of whether or not a urethral sling is present. (HENDRIXM_CMCENTE_121-25).

In 2011, Dr. Franke saw Ms. Hendrix. Physical examination noted that the TVT sling was easily palpable and covered by a very thin layer of epithelium in one area. An area of mesh erosion was deemed to possibly be present. The notes from this exam included these entries: "I tried to examine this area visually, but could never actually see this to confirm it [an erosion]. If she does have a vaginal erosion, it is very minimal, and clearly could be a source of infection. She denies any vaginal spotting or discharge. She does have dyspareunia." Dr. Franke recommended non-operative management including continuing the use of Elmiron, Bactrim DS and Estrace cream. Of note is that in postmenopausal women, thinning of the vaginal epithelium occurs due to loss of the estrogen effects. This impairs vaginal blood flow and causes atrophic changes. As would be expected, any graft placed under the vaginal epithelium would be more palpable (biologic or mesh related). This is not a consequence unique to mesh but can be appreciated with any graft used for either pelvic prolapse or incontinence. (HENDRIXM_PENUR_14, 13-VUMC_565, 564).

Ms. Hendrix returned to Dr. Franke's clinic on April 5, 2011, complaining symptoms of cystitis for the preceding week. A urine culture showed greater than 100,000 CFU/ml Klebsiella. An antibiotic (Ceftin) was prescribed. Later Ms. Hendrix reported that she developed rash and eye swelling after taking this medication. (HENDRIXM_PENUR_13, 97, 31, 12). A urine specimen obtained on April 5th

showed zero to two white cells without red cells or bacteria. Dr. Franke recommended that Ms. Hendrix continue Elmiron and Estrace, use Trimethoprim as suppressive therapy for UTI, and return for follow-up in two months. Of importance here is the use of Elmiron to treat Ms. Hendrix. The treating physician believes, as I do, that her chronic urinary symptoms reflect an underlying PBS/IC condition for which Elmiron is an FDA approved oral medication. As mentioned previously, placement of a sling or any pelvic prolapse procedure in a patient with PBS/IC will often have increased symptoms of urinary urgency and frequency thereafter.

Ms. Hendrix returned to see to Dr. Franke on June 21, 2011. She said that she had recently sought care in an ER because of fever and abdominal cramping. Reportedly a urinalysis done at the time of this ER visit showed mixed flora consistent with a contaminant. Ms. Hendrix said she was dehydrated when she went to the ER but after receipt of several liters of IV fluids, she felt better. Urine studies did not support a diagnosis of a urinary tract infection during her June 21st visit to Dr. Franke's office. Dr. Franke recommended that Ms. Hendrix take probiotics and that she keep a previously scheduled appointment with her gastroenterologist. (HENDRIXM_VUMC_472). That appointment occurred on July 5, 2011. Ms. Hendrix's complaints at that time included abdominal pain and pain from her "neck to her pelvic area." She said that these symptoms started while she was taking antibiotics for repeated UTIs in December 2010. Her gastroenterologist recommended that she undergo colonoscopy. As mentioned previously, patients with PBS/IC often have a constellation of other medical problems and can include the gastrointestinal system with conditions such as GERD and Irritable Bowel Syndrome. When these other systems are involved, the bladder symptoms that

these patients can worsen as well. Thus, increases in urinary urgency, frequency and pelvic pain can occur. This may be the case with Ms. Hendrix. (HENDRIXM_BLUG_40-43).

Ms. Hendrix saw Dr. Melissa Kaufman, an urologist at Vanderbilt University, on July 27, 2011. Her chief complaint at the time of this visit was recurrent UTIs, pressure, and dyspareunia. Dr. Kaufman conducted an exam and recommended cystoscopy and video urodynamics. Examination revealed urethral hypermobility and the urethra and bladder were not tender to palpation. The vaginal mucosa was healthy without evidence of mesh extrusion. Her PVR was 31 cc. Ms. Hendrix indicated on the standard intake form used in Dr. Kaufman's office that she had or was currently having difficulty with radiation treatments. Dr. Kaufman subsequently commented that radiation treatments can impact lower urinary tract function. (HENDRIXM_VUMC_526; Dr. Kaufman depo. at 36). This is an important point to consider as mentioned above. Radiation cystitis is a common cause of refractory urinary urgency, frequency and pelvic pain. Recurrent UTI and dyspareunia can also occur with radiation cystitis. Ms. Hendrix returned to see Dr. Kaufman August, 19, 2011. Urodynamic evaluation revealed a bladder capacity of 283 cc. She again voided with a very slow urinary flow rate and exhibited no post void residual. Cystoscopy revealed nodules within the bladder consistent with "cystitis cystica" (which Dr. Kaufman later said in her deposition testimony is very common in post-menopausal women). There was no evidence of mesh erosion into the urinary tract. (HENDRIXM_VUMC_438-440; Dr. Kaufman depo. at 37-38). Although Ms. Hendrix told Dr. Kaufman that she knew she had UTIs, a urinalysis did not show findings suggestive of infection. Dr. Kaufman discussed treatment options with Ms. Hendrix.

These included removal of mesh and continuation of suppressive antibiotic therapy. Ms. Hendrix decided to have her mesh removed. Dr. Kaufman told her that mesh removal may not resolve her symptoms, pain, infections, or voiding dysfunction, and also that her stress urinary incontinence was likely to recur. (HENDRIXM_VUMC_428). Later in her deposition, Dr. Kaufman explained how it was possible that urinary tract infections could still occur after the mesh was removed:". . . the mesh was not the culprit of causing the urinary tract infections or that (the urinary tract infections) were not urinary tract infections at all but bladder instability, which mimics urinary infection in women." (Dr. Kaufman depo. at 41).

On November 29, 2011, Dr. Kaufman removed a portion of the mesh, but allowed the "wings" to remain. Dr. Kaufman explained this further in her subsequent deposition: "[U]nless there is an active area of purulence or obvious infection that's emanating from those areas, we do not endeavor to remove those meshes out of those deep tissue layers where they're anchored...." (Dr. Kaufman depo. at 45). Dr. Kaufman further stated that she did not see any signs of infection warranting removal of the wings and did not see any mesh erosion. (HENDRIXM_VUMC_375-76; Dr. Kaufman depo. at 45). The surgical pathology report of excised mesh was unremarkable. (HENDRIXM_VUMC_269; Dr. Kaufman depo. at 48).

Ms. Hendrix returned to see Dr. Kaufman approximately two months following the preceding surgery (2/1/12). She reported that she continued to suffer from the same complaints she had pre-operatively. These included burning, frequency, pain, pressure, urinary tract infection symptoms, and urgency. She also reported that her stress urinary incontinence had returned as Dr. Kaufman had warned her it would if she chose to have

her mesh explanted. (HENDRIXM_VUMC_136-37). A urinalysis was negative. Dr. Kaufman cautioned Ms. Hendrix regarding her use of multiple antibiotics and discussed possible alternate modalities of treatment for her continued symptoms of voiding dysfunction, including Botox injections. (HENDRIXM_VUMC_136-137). This indicates that Dr. Kaufman recognized the chronic nature of Ms. Hendrix's voiding symptoms and referred to them as refractory urgency and frequency (also known as PBS/IC) and has recommended appropriate treatments for this condition including sacral neuromodulation or onabotulinum toxin A (Botox). Of note is that these treatments are second and third line methods and are utilized for patients with chronic, longstanding symptoms such as those exhibited by Ms. Hendrix.

After more than a three-year gap and shortly before Dr. Kaufman's deposition in this case, Ms. Hendrix returned to see Dr. Kaufman on November 18, 2015. Her chief complaint was stress urinary incontinence with pain. Dr. Kaufman's exam revealed atrophic vaginitis, no discharge, masses, or lesions, otherwise unremarkable. A urinalysis was negative. Dr. Kaufman recommended that Ms. Hendrix proceed with transvaginal estrogen to reduce her incidence of UTIs and counseled in the use of coconut oil in the interim. (HENDRIXM_KAUFMANDEPO_ 1-4). She also continued to recommend either Botox injections or placement of an InterStim device. These recommendations further confirm the presence of PBS/IC in this patient.

II. Case Specific Opinions

Ms. Hendrix was an appropriate candidate for surgery to treat her SUI. She was appropriately worked up prior to surgery with history, physical examination, urodynamics, and cystoscopy and was counseled extensively. Her SUI was bothersome,

having returned in 1998 or 1999 after her Marshall-Marchetti procedure, performed in 1986, failed. She reported that the condition had worsened in the two years before her TVT implant, and she was forced to wear panty liners.

Decisions regarding the best treatment for SUI are made by a woman and her doctor. Ms. Hendrix consented to the procedure after discussing her treatment options with Dr. Hubbard.

Dr. Hubbard was aware of the risks and complications associated with the TVT procedure and according to his testimony and the medical records, he discussed those risks and potential complications with Ms. Hendrix in detail and gave her the opportunity to ask any questions.

Dr. Hubbard is an experienced urologist who has performed synthetic MUS procedures for many years. He was well trained and was well-aware of the risks and complications of pelvic floor surgery including TVT. His medical records reflect these discussions with Ms. Hendrix.

At the time of this implant in 2006 there were no procedures or products that were safer and more effective than TVT, and its benefits exceeded its risks for Ms. Hendrix. The product was both safe and effective for her. Her stress urinary continence was resolved after the implant, as documented in the medical records, including those of Melissa Kaufman, MD. It did not return until she had her mesh explanted (all but the wings), and she had been warned by Dr. Kaufman that recurrence was likely if she chose to have the sling removed. Further, recurrence is a risk of any SUI procedure, whether or not mesh is used, and Ms. Hendrix was well aware of that possibility, as her SUI recurred

after her MMK procedure. There is no evidence that the TVT placed in Ms. Hendrix had eroded or penetrated into her bladder or urethra.

Further, after Ms. Hendrix's mesh was removed by Dr. Kaufman, the mesh removal did not change her preoperative symptoms, according to Dr. Kaufman's office notes. Even with antibiotics, Ms. Hendrix had minimal relief of her symptoms. This suggests that the sling was not the cause of her urinary symptoms. The fact that antibiotics did not help her points to an underlying sensory neuropathic bladder as the prevailing reason for her chronic urinary symptoms. This is further suggested by cystoscopic findings of chronic cystitis cystica. Ms. Hendrix has urodynamic evidence of a sensory neuropathic bladder. This condition by itself is associated with chronic symptoms of urinary urgency, frequency and dysuria. Her urodynamic studies of July 12, 2006, reveal a physiologic bladder capacity of only 200 cc. She voids with a very low urinary flow rate of 5 cc/sec. Her bladder capacity is small. Ms. Hendrix's subsequent urodynamic studies performed by Drs. Hubbard and Kaufman confirmed the above findings of a small capacity bladder with sensory urgency.

Ms. Hendrix's persistent voiding dysfunction with symptoms of urinary urgency, frequency and UTIs may be related to her MMK procedure. Review of the operative note from that procedure indicates that 0" Vicryl sutures were used with a total of 7 sutures placed (including the right and left sides of the urethra to the pubic bone). Such sutures, especially when of the permanent type, can cause postoperative voiding symptoms such as urinary urgency and frequency. Cystoscopy was not performed at the time of the procedure. Complications of MMK procedures can be significant and can include

enterocutaneous fistula, osteitis pubis, and persistent voiding dysfunction in 5-20% of patients.

Ms. Hendrix complained of dyspareunia. However, she only mentioned this twice in her extensive medical history. One time was in 2007 to Dr. Katz and the other time was upon presentation to Dr. Kaufman in 2011. If this were a significant problem for her she surely would have mentioned it more frequently to her treating physicians, and pertinent findings of mesh extrusion would be noted on physical examination. No such findings of mesh extrusion were ever noted by any of her treating physicians. In addition, dyspareunia is often found in post menopausal women, whether or not they have had surgery with mesh. Ms. Hendrix is post menopausal, diagnosed with atrophic vaginitis and was advised to use lubricants and creams (which may or may not alleviate dyspareunia symptoms).

Ms. Hendrix has periodic complaints of frequency, urgency, and burning with urination, which she interprets as urinary tract infections. She has in fact reported burning with urination and urinary tract infections years before her mesh was implanted. Further, UTIs are among the most common infectious diseases worldwide, and there can be a myriad of causes for UTIs, as reflected in the case specific report of Dr. Sexton, which I have read and with which I agree. Further, post-menopausal women like Ms. Hendrix who have estrogen depletion because they do not take estrogen therapy (she has breast cancer) are at increased risk for UTIs.

Ms. Hendrix has a number of significant medical problems including breast cancer treated with surgery and radiation. This condition by itself can be associated with refractory urinary urgency and frequency. She has a history of peripheral

neuropathy. Neuropathic conditions in other parts of the body can be associated with neuropathy involving the bladder. Ms. Hendrix has a history of Raynaud's syndrome, Rheumatoid Arthritis, and an ill-defined connective tissue disease disorder. These conditions are associated with a condition known as Painful Bladder Syndrome/Interstitial Cystitis. This condition is likely in Ms. Hendrix given her chronic urinary urgency and frequency which has existed over many years. This is further suggested by the manner in which she was treated using medications such as pentosan polysulfate (Elmiron) and being offered treatments such as sacral neuromodulation (Interstim) and botulinum toxin A (Botox) injections. This condition can exist in the presence or absence of chronic urinary tract infections.

I see no evidence in the records of alleged mesh problems such as roping, curling, degradation, cytotoxicity or cancer.

III. Rebuttal of Expert Witness Deposition Testimony

Dr. Steege correctly mentions that Ms. Hendrix complains of "longstanding bladder dysfunction and recurrent infections." He states that she underwent total abdominal hysterectomy and modified MMK for treatment of SUI on May 13, 1986. Her voiding issues have been problematic for many years. Dr. Steege does not mention the details of the MMK procedure which placed a total of approximately 7 zero-vicryl sutures in the periurethral tissues to elevate the urethra. He does not acknowledge the significant and persistent voiding dysfunction that can occur post operatively in up to 20% of patients. This likely occurred in Ms. Hendrix. Further, Dr. Steege does not mention that Ms. Hendrix was 32 years of age when she had her procedure. Given her

young age at surgery, she is at high risk of failure of the MMK over time which ultimately occurred.

Dr. Steege notes that since her sling placement on September 14, 2006, she has had apparently new dyspareunia and has struggled with multiple recurrent UTIs as well as bladder irritability in the absence of infection. Dr. Steege did not mention that Ms. Hendrix's history of bladder irritability and recurrent UTIs predated the TVT placed by Dr. Hubbard. These symptoms likely began after her MMK many years ago.

Dr. Steege mentioned that cystoscopy showed a degree of apparent outflow obstruction but no erosion of the ureter by the mesh. Dr. Steege failed to note that this outflow obstruction predated the TVT placement. This was evidenced by the +1/+3 bladder trabeculation on initial cystoscopy performed by Dr. Hubbard prior to placement of the TVT. This outflow obstruction is likely the result of her MMK procedure which resulted in bladder outlet obstruction. Further, as mentioned previously, suture placement into the lateral aspects of the urethra as part of the MMK procedure can result in chronic urinary urgency, frequency and pelvic pain.

Dr. Steege mentions dyspareunia as a new complaint on August 7, 2007. It is important to note that in only two notes in Ms. Hendrix's medical record (the note of Dr. Katz October 7, 2008, and Dr. Melissa Kaufman July 27, 2011) is dyspareunia mentioned. This underscores that this issue is not significant for this patient or she would have mentioned it more frequently to her treating physicians.

Dr. Steege mentioned in list form the significant medical problems and past surgical history for Ms. Hendrix. However, he failed to make the connections between her rheumatoid arthritis, peripheral neuropathy, ill-defined connective tissue disorder,

radiation treatments and her prior MMK procedure to the presence of longstanding irritative voiding symptoms consistent with PBS/IC. This is a major flaw in his case specific review as the additive effects of these conditions certainly explain the symptoms of Ms. Hendrix.

Dr. Steege mentioned that Ms. Hendrix developed significant bladder symptoms following TVT mesh placement. He further goes on to say that these symptoms persisted despite attempted removal of the mid portion of the mesh. This reasoning is faulty on several levels. First, as mentioned, Ms. Hendrix had significant issues with urinary urgency and frequency for many years prior to her TVT placement. I have already discussed reasons for this in detail including her small bladder capacity, and significant relevant medical history (rheumatoid arthritis, peripheral neuropathy, ill-defined connective tissue disorder, radiation treatments and her prior MMK procedure). Further, the fact that her symptoms persisted after removal of the mesh suggests that her irritative voiding symptoms are unrelated to the TVT. First, her symptoms predated the TVT placement and second, they persisted after the TVT was removed. Her symptoms likely relate to PBS/IC and her MMK.

Dr. Steege states that as a result of complications from the TVT, Ms. Hendrix suffered and continues to suffer injuries. This reasoning is incorrect for reasons described above. Further, this patient had no evidence of mesh erosion or extrusion. As discussed, the patient's irritative voiding symptoms predated the TVT and likely began at the time of or thereafter her MMK procedure. The relationship between her significant medical problems and PBS/IC cannot be understated as they are certainly related.

Conclusion:

In conclusion, from the review of the materials, including medical records and deposition transcripts, there is no objective or subjective evidence to suggest that the mesh characteristics of the TVT sling are the cause of Ms. Hendrix's issues. Her sling was appropriately placed in the surgical procedure with no subsequent findings of erosion or extrusion. My opinions are stated to a reasonable degree of medical certainty.

Stanley Zaslau, M.D., MBA, FACS